B. Environmental Factors.

a. The major risk factor to papillary thyroid cancer is exposure to ionizing radiation, during the first 2 decades of life.

b. Deficiency of dietary iodine:

- Is linked with a higher frequency of follicular carcinomas.

1. **Papillary Carcinoma :**

- Is most the most common form
- accounts for the majority of thyroid carcinomas associated with previous exposure to ionizing radiation.
- The most common thyroid cancer in children
- May occur at any age,

Gross: Either solitary or multifocal lesions

Microscopically

1. The nuclei of papillary carcinoma cells

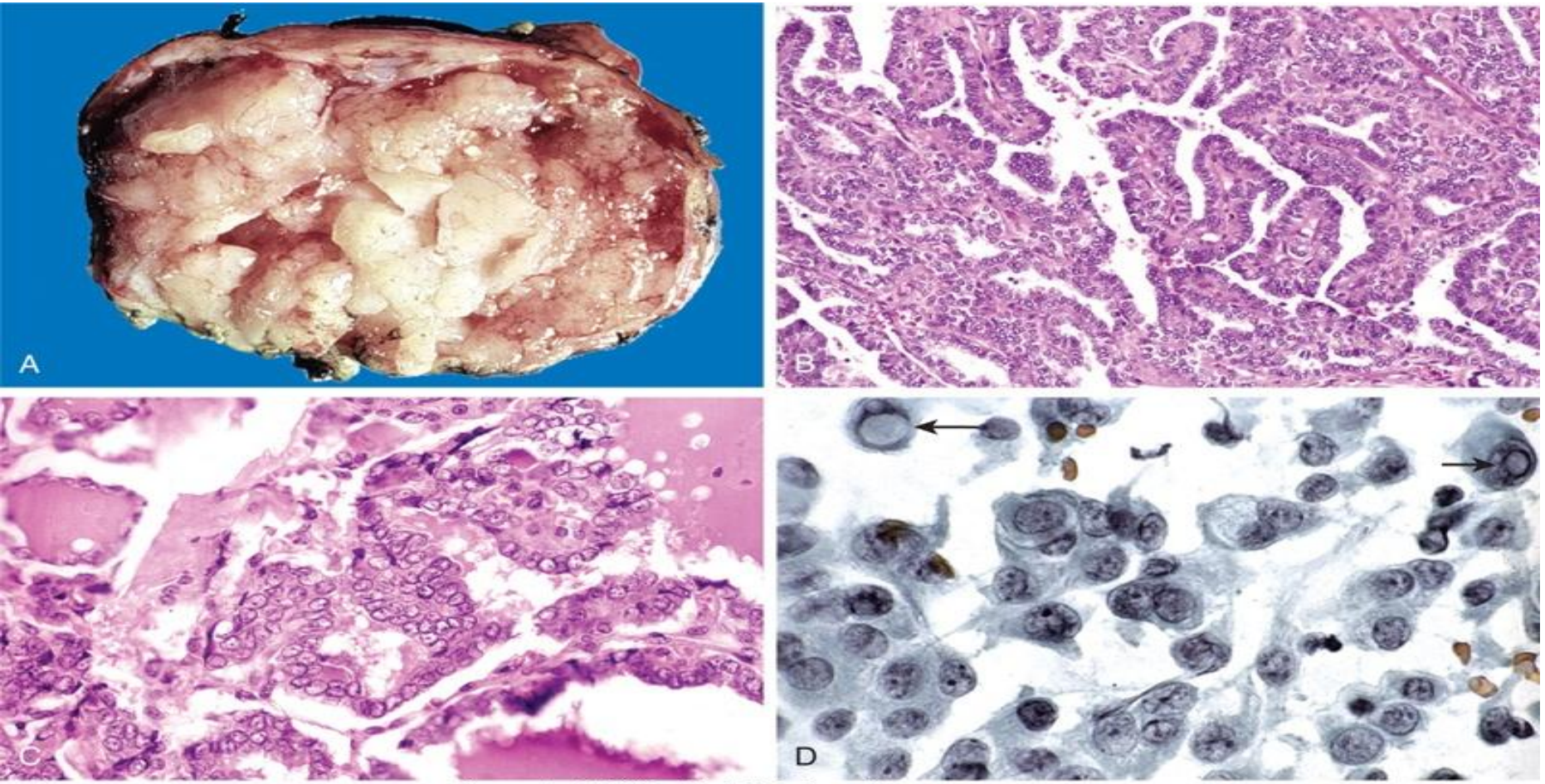
a.are optically clear nuclei, or "Orphan Annie eye" nuclei.

b. Have pseudoinclusions)

2. A papillary architecture is common
3. Concentrically calcified structures(psammoma bodies)
4. Foci of lymphatic permeation by tumor cells are present, with metastases to cervical lymph nodes in half of cases.
5. but invasion of blood vessels is uncommon

Variants: The most common is follicular variant associated with a lower incidence of lymph node metastases and extrathyroidal extension than that for conventional type

Papillary carcinoma



Clinical Features of papillary carcinomas

a. Are nonfunctional tumors manifest as painless mass in the neck, either within the thyroid or as metastasis in a cervical lymph node

b. Are indolent lesions, with 10-year survival rates of 95%.

c. The presence of isolated cervical nodal metastases does not have a influence on good prognosis of these lesions.

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d. In a minority of patients, hematogenous metastases are present at the time of diagnosis, most commonly to lung

- The bad prognostic factors are:

a. Tumors arising in patients older than 60

b. The presence of extrathyroidal extension

c. Presence of distant metastases (stage)

2. Follicular Carcinoma :

-- More common in women and in areas with dietary iodine deficiency (accounting for 25% to 40% of thyroid cancers in these regions).

- The peak incidence between the ages of 40 and 60 years

Pathologically It may be

a. Widely invasive, infiltrating the thyroid parenchymaand extrathyroidal soft tissues, or

b. Minimally invasive that may be impossible to distinguish from follicular adenomas on gross examination and

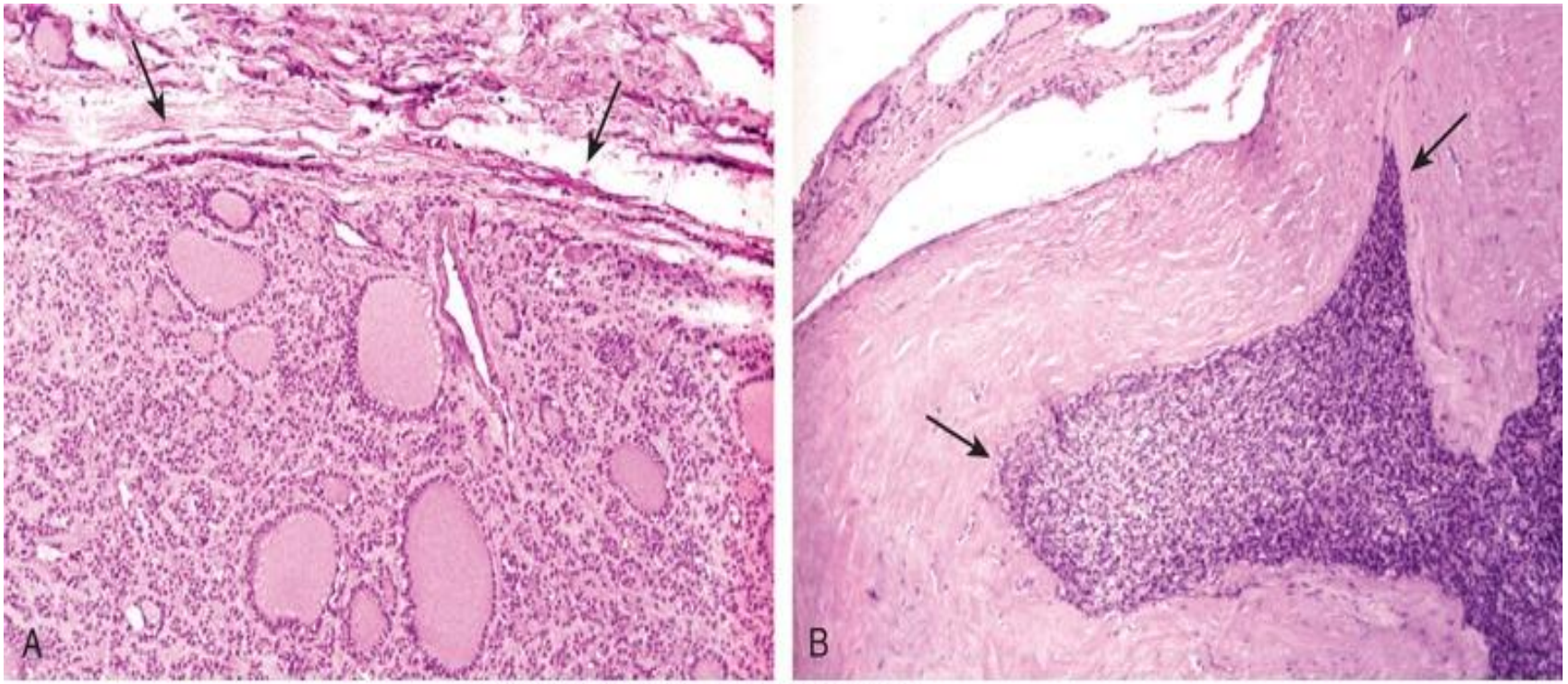
.

and/or vascular invasion to differentiate it from follicular adenoma

Clinical Features

- Manifest frequently as solitary *cold thyroid nodule.*
- Tend to metastasize through h*ematogenous routes* to lungs, bone, and liver but uncommon regional nodal metastases are uncommon .
- Half of patients with widely invasive carcinomas succumb to their disease within 10 years,
- less than 10% of patients with minimally invasive follicular carcinomas die within the same time span.

Follicular carcinoma



- Are treated with surgical excision.
- Because better-differentiated lesions may be stimulated by TSH, patients usually are placed on a thyroid hormone regimen after surgery to suppress endogenous TSH.

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3. Anaplastic Carcinoma

- Are undifferentiated tumors of the thyroid epithelium, with mean age of 65 years.
- They are aggressive, with a mortality rate of 100%.
- Approximately 1/4th of patients have a past history a well-differentiated carcinoma, and harbor a well-differentiated tumor in the resected specimen
- Metastases to distant sites are common, but death occurs in less than 1 year as a result of aggressive local growth which compromise of vital structures in the neck.

4. Medullary Carcinoma

- Are neuroendocrine neoplasms.
- Secrete calcitonin, the measurement of which plays an important role in the diagnosis and postoperative follow-up evaluation of patients.
- In some cases, the tumor cells elaborate , serotonin, and vasoactive intestinal peptide (VIP)
- Are sporadic in about 70% of cases
- 30% are *familial* cases

a. Occurring in the setting of MEN syndrome 2A or 2B, have been reported in younger patients, including children

b. or familial medullary thyroid carcinoma without an associated MEN syndrome

Note: Both familial and sporadic forms demonstrate activating *RET* mutations.

- Sporadic medullary carcinomas, as well as familial cases without an associated MEN syndrome, occur in adults , with a peak incidence in the fifth and sixth decades.

. MORPHOLOGY

- Multicentricity is particularly common in familial cases.

On microscopic examination,

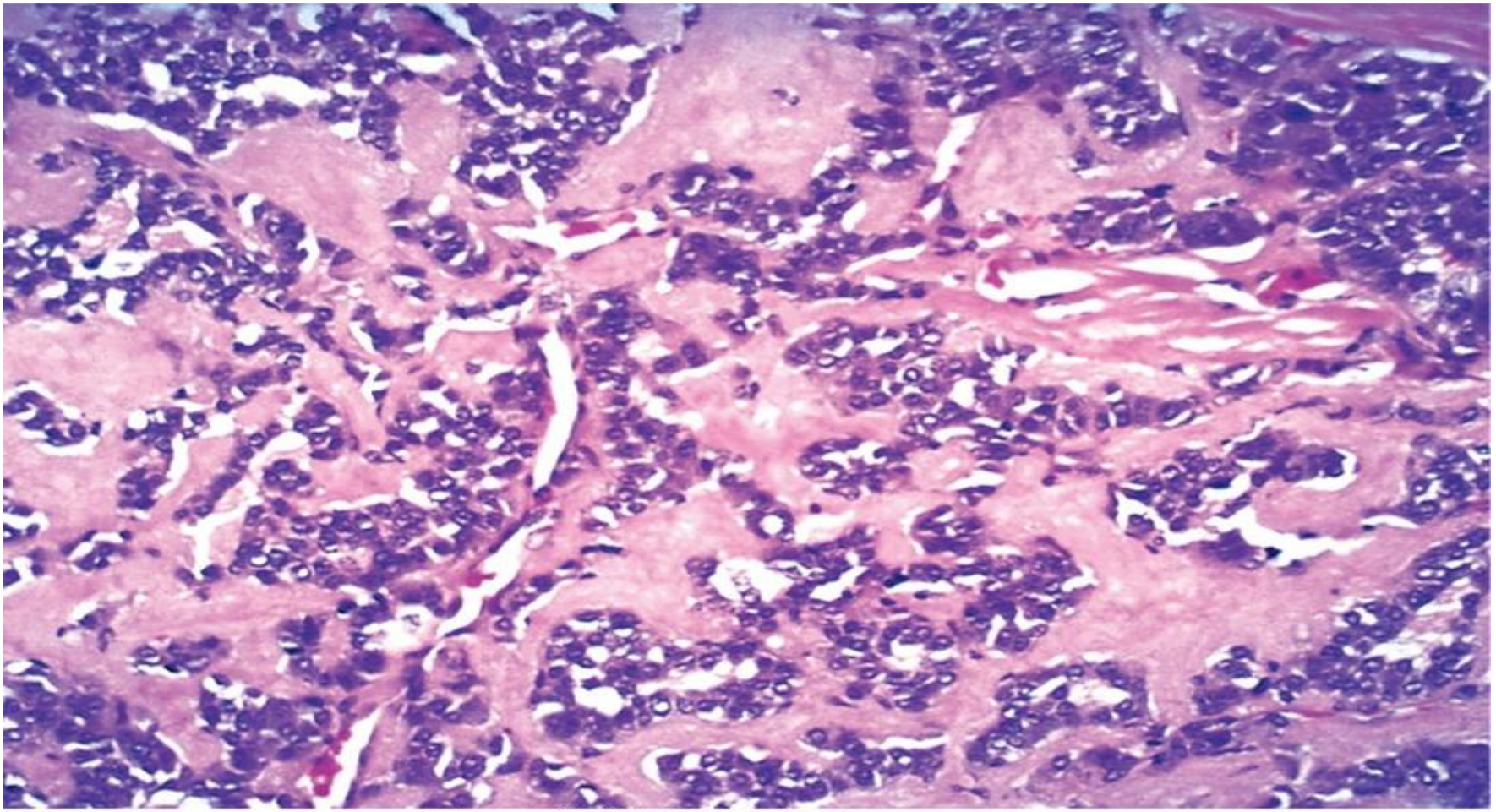
- The tumor cells may form nests, trabeculae, and even follicles.
- Amyloid deposits, derived from calcitonin molecules, are present in the adjacent stroma in many cases
- Calcitonin is readily demonstrable both within the cytoplasm of the tumor cells or amyloid

- Familial cases are characterized by the presence of multicentric C cell hyperplasia in the surrounding thyroid parenchyma, a feature usually absent in sporadic lesions.
- And these foci are believed to represent the precursor lesions from which medullary carcinomas arise

Clinical Features

- The sporadic cases manifests most often as a mass in the neck, sometimes associated with dysphagia or hoarseness.

Medullary carcinoma



- In some instances, the initial manifestations are caused by the secretion of a peptide hormone (e.g., diarrhea caused by the secretion of VIP).
- Screening of the patient's relatives for elevated calcitonin levels or *RET* mutations permits early detection of tumors in familial cases
- All members of MEN-2 kindreds carrying *RET* mutations are offered prophylactic thyroidectomies to prevent the development of medullary carcinomas

- Often, the only finding in the resected thyroid of these asymptomatic carriers is the presence of C cell hyperplasia or small (<1 cm) *micromedullary* carcinomas.

II. Parathyroid gland

I. HYPERPARATHYROIDISM : 3 categories

a. Primary Hyperparathyroidism

- Is a common disorder and important cause of hypercalcemia
- There has been an increase in the detection of cases as a result of the routine inclusion of serum calcium assays in testing for a variety of clinical conditions

Causes of primary hyperparathyrpoidism

1. Parathyroid adenoma (85% to 95%)
2. Primary parathyroid hyperplasia-5% to 10%.
3. Parathyroid carcinoma-(1%)

Genetic changes in parathyroid adenoma

1. Cyclin D1 is overexpressed in 40% of adenomas,
2. MEN1 mutations: About 20% to 30% of parathyroid tumors not associated with the MEN-1 syndrome have mutations in both copies of the *MEN1* gene

Primary hyperparathyroidism

- is a disease of adults and is much more common in women than in men.
- *The most common manifestation is an increase in serum calcium and i*s the most common cause of *clinically silent hypercalcemia.*
- The most common cause of clinically apparent hypercalcemia in adults is

a. paraneoplastic syndromes associated with *malignancy*

b. and bone metastases

Lab findings

a- In persons with hypercalcemia caused by parathyroid hyperfunction, serum PTH is inappropriately elevated

b. in hypercalcemia due to non parathyroid diseases, serum PTH is low to undetectable

c. Hypophosphatemia

d. Increased urinary excretion of calcium and phosphate

Clinical Manifestations :

- Traditionally has been associated with a constellation of symptoms "painful bones, renal stones, abdominal groans, psychic moans.“

1. Pain was at one time a prominent manifestation of primary hyperparathyroidism and is secondary to

a. Fractures of bones

b. and resulting from renal stones

c. Pancreatitis and gall stones

d. Peptic ulcer

Note;

- Because serum calcium is now routinely assessed in the most patients who need blood tests for other conditions, clinically silent hyperparathyroidism is detected early.
- Hence, many of the classic clinical manifestations, , are seen much less frequently .

2. *Gastrointestinal disturbances,* including constipation, nausea, peptic ulcers, pancreatitis, and gallstones

3. *CNS alterations,* - depression, lethargy, and seizures
4. *Neuromuscular abnormalities,*- weakness and hypotonia
5. *Polyuria* and secondary polydipsia